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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,514	11/17/1998	MIE KAINOH	1102-98	8751

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IP DEPARTMENT OF PIPER RUDNICK LLP
3400 TWO LOGAN SQUARE
18TH AND ARCH STREETS
PHILADELPHIA, PA 19103

EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/02/2003

38

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/155,514	KAINOH ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-9,50 and 51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-9,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/3/2003 has been entered.

2. Claims 3-9,25,50,51 are under consideration. Claims 3 and 25 have been amended. Claim 2 has been cancelled. Claims 50,51 are newly added.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 51 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the claimed invention. Claim 51 encompasses peptides wherein the two peptides are linked by disulfide bounds found at positions other between the two Ig heavy chain portions of the molecule. While the particular portions of the specification cited by applicant disclose heterodimers linked by disulfide bond connecting the two Ig heavy chain molecules, they do not disclose that the disulfide bond occurs between the nonIg heavy chain portion of the molecule as encompassed by claim 51. The written description provided in the specification is not commensurate with the scope of the claimed invention (eg. the claimed invention constitutes new matter).

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 2-9,25,50,51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carter et al. (US Patent 5,821,333) in view of Hori et al. (US Patent 5,916,771) and Presta et al.(US Patent 6,025,166) and prior art disclosed in the specification (see references disclosed in pages 2 and 3 of the specification).

Carter et al. teach recombinant fusion proteins containing an adhesion molecule linked to a constant heavy chain derived from an Ig molecule (see columns 19 and 20). Carter et al. teach that said molecules are bispecific immunoadhesions (see column 19). Said molecules need to have two functioning chains in order to function as a bispecific immunoadhesion. Carter et al. teach that such molecules can be dimers, wherein the two chains contain different adhesion molecules wherein the two adhesion molecules are both fused to heavy chain Ig constant regions (see column 19, last paragraph, continued on next page). Carter et al. do not specifically teach that the adhesion molecules are derived from an α and β chain of an integrin or are linked by a disulfide bond between the Ig heavy chains. Hori et al. teach that β_1 integrin molecules were known in the art as heterodimeric molecules (see column 5). The prior art disclosed in the specification, pages 2 and 3 indicates that integrin molecules and the integrin chains recited in the claims were known in the art. The prior disclosed in the specification, page 3 indicates that β_1 integrin molecule was known in the art as heterodimeric molecule containing a β_1 and an $\alpha 4$ chain. Carter et al. teach that Ig fusion proteins have a variety of art recognized uses (see column 4). Carter et al. disclose that Ig heavy chain is fused to the C-terminal of the adhesin (see column 19, first paragraph and last paragraph). Hori et al. teach recombinantly produced dimeric integrin molecules (see column 5). Carter et al. also teach recombinantly produced dimeric adhesion molecules (see columns 19 and 20). Carter et al. teach that the heterodimers are linked, but not the specific nature of the linkage. Presta et al disclose Ig fusion molecule heterodimers that contain two Ig heavy chains wherein the molecules are linked by a disulfide bond (see column 5, first paragraph) and that the construct contains cysteines in the heavy chain which mediate formation of disulfide bonds between the two heavy chains (see column 36, first paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Carter et al. teach recombinant fusion proteins containing an adhesion molecule linked to a constant heavy chain derived from an Ig molecule while Hori et al. teach that β_1 integrin molecules were known in the art as heterodimeric molecules and that such molecules can be recombinantly

produced whilst Presta et al disclose Ig fusion molecule heterodimers that contain two Ig heavy chains wherein the molecules are linked by a disulfide bond (see column 5, first paragraph) and that the construct contains cysteines in the heavy chain which mediate formation of disulfide bonds between the two heavy chains. One of ordinary skill in the art would have been motivated to do the aforementioned because Carter et al. teach that Ig fusion proteins have a variety of art recognized uses (see column 4). Carter et al. teach use of Ig fusion proteins as drugs (see column 4). The various integrin molecules recited in the claims were all known in the art. Human Ig heavy chain sequences are known in the art (see Carter et al., columns 18 and 19).

Regarding applicants comments, Carter et al. is an issued US Patent which contains claims drawn to recombinantly produced heteromultimeric peptides. The claims of an issued US Patent are considered valid and enabled. Therefore the molecules taught by Carter et al. are expected to retain the binding function of the parent integrins. The molecules are also stably associated (eg. via disulfide bonds). Presta et al disclose Ig fusion molecule heterodimers that contain two Ig heavy chains wherein the molecules are linked by a disulfide bond (see column 5, first paragraph) and that the construct contains cysteines in the heavy chain which mediate formation of disulfide bonds between the two heavy chains (see column 36, first paragraph). Regarding applicants comments about Kainoh et al., Kainoh et al. addressed functional/stability issues via a fusion protein with the Ig heavy chains covalently linked. Presta et al disclose Ig fusion molecule heterodimers that contain two Ig heavy chains wherein the molecules are linked by a disulfide bond (see column 5, first paragraph) and that the construct contains cysteines in the heavy chain which mediate formation of disulfide bonds between the two heavy chains (see column 36, first paragraph). Therefore, the protein rendered obvious in the instant rejection has the same properties as the claimed invention because it is the same protein. Regarding the binding domain of the integrin, immunoadhesion fusion proteins containing the binding domain of a known molecule were well known in the art (see column 4, second paragraph).

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1602